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WO-A-87/00086
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Description

This invention relates to bio-fluid assay apparatus of the kind (hereinafter termed of the kind referred to) wherein measured samples of bio-fluid, for example serum, are introduced into the wells of a microtitre plate (hereinafter 'plate') for subsequent chemical reaction and analysis.

A principal use of apparatus of the kind referred to is the carrying out of immuno-assay tests of serum, the wells of the plates being dosed with antibodies appropriate to the tests to be performed, suitable chemical reagents then being added prior to incubation washing and reading.

WO 87/00086 discloses bio-fluid assay apparatus comprising a micro-processor controller, a plurality of discrete carriers, a magazine for said carriers, a plurality of operational stations including:
a station where reagents are added
a washing station
a plate reading station
each plate carrier having a uniquely identifying machine readable label and
transport means including means for reading said labels to allow for a proper handling of the analysis system. In this arrangement, however, excluding incubation in the magazine only one plate can be operated on at any one time and this severely restricts throughput.

EP-A3-0185330 and EP-A3-0192968 each disclose the provision of machine readable labels for control of proper handling of liquid samples.

According to the present invention, there will be provided a bio-fluid assay apparatus wherein measured samples of bio-fluid in the wells of a microtitre plate are analysed comprising:

a micro-processor controller which may be input with details of patients and different tests required;

a plurality of discrete plate carriers;

a magazine for said carriers;

a plurality of operational stations including:

a station where chemical reagents are added to the plates by a reagent dispensing arrangement;

a plate washing station;

a plate reading station;

plate carrier transport means which is controlled by the micro-processor for collecting plate carriers from said magazine and progressing them as required through the operational stations;

each plate carrier having a uniquely indentifying machine readable label which by reference to the data held by the micro-processor will indicate the particular type of the assay to be effected on the samples carried by the plate;

the transport means including means for reading said labels whereby the micro-processor control means can verify that each carrier taken from the magazine was loaded and is selected correctly and can confirm the validity of other movements during the assay cycle; and

characterised in that the transport means is able to move the plate carriers in either direction along each of the x, y and z axes between the different operational stations in a manner determined by the micro-processor controller which is programmed to determine the order in which different assays are performed.

A first operational station may be a transfer station at which the plates receive measured samples of bio-fluid transferred from a sample receiving section by an automatic pipette arrangement.

The sample receiving section may include a reader for machine readable labels on sample tubes to confirm that such are correctly loaded into the sample receiving section.

The invention will be further apparent from the following description with reference to the figures of the accompanying drawings, which show, by way of example only, one form of bio-fluid assay apparatus embodying same.

Of the drawings:-

Figure 1 shows a perspective diagrammatic view of the bio-fluid assay apparatus according to the invention; and

Figure 2 shows a detail of the reagent dispensing station of the apparatus of Figure 1.

The apparatus is controlled by a suitably programmed micro-processor M, which is input with details of patients and the tests required for example Thyroid, Fertility, Steroid, HIV, Hepatitis and so on. Each test may require a plurality of separate assays. An operator will be directed by the micro-processor to load the apparatus with appropriate plates and samples of the patients' bio-fluids on specified carriers at specified locations. Thereafter the transfer of bio-fluid to the plates and progress of the plates through the various operational stations is under the control of the micro-processor which will give a print-out of all completed test results. In general the micro-processor will determine the order in which different assays will be performed to optimize throughput having regard to different residence time requirements at different operational stations for the different assays and other factors.

Turning now to Figure 1, it will be seen that the apparatus has an input magazine generally indicated at 10 for plate carriers 11 each loaded with a microtitre plate 12, and an output magazine 13 which receives the carriers 11 after they have passed through the various operational stations of the apparatus.

The uppermost tier 10a of the input magazine 10 defines a transfer station at which the wells of

the plates are dosed with measured volumes of bio-fluid transferred thereto by a multi-head automatic pipette arrangement generally indicated at 14 and indexable along the x-axis on rails 15 between the transfer station and a sample receiving section 16 loaded with tubes 17 of sample. The arrangement 14 is also indexable along the y-axis so that the pipette tips can register with any desired wells in a plate located on a carrier at the transfer station. The pipette tips are themselves movable along the z-axis as is obviously necessary for collection and delivery of sample. The pipette tips may be automatically exchanged or washed after each use in known manner. The tubes 17 carry bar-coded labels 18 (preferably printed under control of the micro-processor at the time of data input). A laser bar-code reader 19 which reports to the micro-processor M is provided to verify that the operator has positioned the sample tubes 17 in the receiving section at the locations directed.

Essentially the apparatus includes a plate carrier transfer mechanism comprising a fork 20 advanceable and retractable along the y-axis to engage with the underside of or be withdrawn from beneath a selected plate carrier. The fork 20 moves along the y-axis relative to a support 21 movable upwardly and downwardly along the z-axis relative to a support pillar 22 itself movable from side to side along the x-axis.

In accordance with the invention each of the plate carriers 11 carries a uniquely identifying machine readable label 28 which by reference to the data held by the micro-processor M will indicate the particular type of assay which the plate carried thereby is to undergo. The support 21 carries a reader for the labels 28 and this reader reports to the micro-processor on the identity of each carrier 11 which the fork 20 engages.

In this way the micro-processor can verify that the operator has positioned plate carriers 11 loaded with plates as directed and confirm the validity of other movements during the assay cycle.

Movement of the fork 20 along all three axes is under the control of the micro-processor to collect plate carriers from the input magazine 10 and position them in the transfer station and after they have been dosed with sample move them to a station generally indicated at 23 where reagents appropriate for the assays to be effected are dispensed into the wells of the plates from a rotatably indexable dispensing head 24.

The station 23, shown in more detail in Figure 2, comprises an indexable dispensing head 24 rotatably mounted below a stationary module 43. The head 24 is indexed by commands from the micro-processor M. The head 24 comprises a plurality of arms 46 radially extending from its centre of rotation, each arm having a machine readable label 65 located on the face of the distal end thereof, said label 65 being indicative of the reagent carried. The label 65 is read by a label reader 76 attached to the module 43, which reports to the micro-processor M, enabling verification that the correct reagents are dispensed to the correct wells of each plate presented at the station 23.

Each of the arms 46 comprises a plurality of reagent dispensers in the form of multi-channel pipettes 47. The pipettes 47 are filled from containers of stock reagents, which may be located in the arms 46. Preferably three pipettes each possessing four reagent exit channels are located in each of the arms 46.

The module 43 has a plurality of powered piston plungers 45 located therein and extensible therethrough to engage with the pipettes 47. The plungers 45 are actuated, as directed by the micro-processor after verification of the labels 65 to operate the pipettes 47.

Whilst the reagents are being dispensed the plate carriers remain supported by the fork which executes necessary step movements in the x and y directions.

The fork 20 then moves the plate carrier into an incubator 25 and deposits it for the required residence time before collecting it for transfer to a washer 26 and reader 27 in turn. The incubator may have a variable heat control and may include a refrigerated zone, since it may be desired to carry out the colourmetric stage of some assays, for example the peroxidase catalysed cleavage of 3,3',5,5' -Tetramethylbenzidine Dihydrochloride, at temperatures below room temperature.

The plate carriers may remain supported by the fork whilst in the washer and reader and the fork may execute necessary step movements to enable reading of all wells. Alternatively the plate carriers may be deposited in the washer for a required time and also in the reader if of suitable design. After each plate has been read, the fork 20 transfers it to the output magazine 13 wherefrom it may be retrieved by the operator to enable the used plate to be discarded (or re-read for quality control purposes, for example) a new plate mounted and the carrier repositioned in the input magazine as directed.

The plates engage with the plate carriers such that their position thereon is precisely determined. Equally the plate carriers have projections or grooves which are engageable with complementary formations on the fork and the surfaces which support them at the various operational stations.

The labels 28 and 65 are conveniently magnetically coded and readable by an array of magnetically operable reed switches, but other kinds of label such as bar-coded labels are possible.

Apparatus, according to the invention, may be used, in addition to immuno-assay, in for example, an assay for the cell proliferative potential of bio-fluid. Cells may be seeded in the wells of the microtitre plates and cell growth or proliferation, for example, can be monitored spectrophotometrically after suitable cell staining and washing regimes. In this way, the vaso-proliferative potential of diabetic serum, for example, may be assessed.

It will be appreciated that it is not intended to limit the invention to the above example only, many variations, such as might readily occur to one skilled in the art, being possible, without departing from the scope thereof as defined by the appended claims.

Claims

1. A bio-fluid assay apparatus wherein measured samples of bio-fluid in the wells of a microtitre plate are analyzed comprising:

   a micro-processor controller (M) which may be input with details of patients and different tests required;

   a plurality of discrete plate carriers (11);

   a magazine (10) for said carriers;

   a plurality of operational stations including:

   a station (23) where chemical reagents are added to the plates by a reagent dispensing arrangement;

   a plate washing station (26);

   a plate reading station (27); plate carrier transport means (20) which is controlled by the micro-processor for collecting plate carriers from said magazine and

   progressing them as required through the operational stations;

   each plate carrier having a uniquely indentifying machine readable label (28) which by reference to the data held by the micro-processor will indicate the particular type of the assay to be effected on the samples carried by the plate;

   the transport means including means for reading said labels whereby the micro-processor control means can verify that each carrier taken from the magazine was loaded and is selected correctly and can confirm the validity of other movements during the assay cycle; and

   characterised in that the transport means is able to move the plate carriers in either direction along each of the x, y and z axes between the different operational stations in a manner determined by the micro-processor controller which is programmed to determine the order in which different assays are performed.

2. Apparatus according to claim 1, further including a transfer station (10a) at which plates receive measured samples of bio-fluid transferred from a sample receiving section (16) by an automatic pipette arrangement (14).

3. Apparatus according to claim 2, wherein the sample receiving section includes a reader (19) for machine readable labels (18) on sample tubes (17) to confirm that such are correctly loaded into the sample receiving section.

4. Apparatus according to any preceding claim, further comprising an incubator station (25).

Patentansprüche

1. Biofluid-Prüfgerät, bei dem gemessene Proben von biologischer Flüssigkeit in den Vertiefungen einer Mikrotiter-Platte analysiert werden, welches aufweist:

   ein Mikroprozessor-Steuergerät (M), in das Details von Patienten und erforderlichen unterschiedlichen Prüfungen eingegeben sein können;

   eine Mehrzahl von einzelnen Plattenträgern (11);

   ein Magazin (10) für die Träger;

   eine Mehrzahl von Arbeitsstationen, enthaltend:

   eine Station (23), in der chemische Reagenzien durch eine Reagensausgabeanordnung zu den Platten hinzugefügt werden;

   eine Plattenwaschstation (26);

   eine Plattenlesestation (27);

   Platten-Transportmittel (20), die vom Mikroprozessor gesteuert werden zum Aufnehmen von Plattenträgern aus dem Magazin und zu deren Beförderung in geforderter Weise durch die Arbeitsstationen;

   wobei jeder Plattenträger ein einmalig identifizierendes, maschinenlesbares Etikett (28) hat, welches durch Bezugnahme auf die im Mikroprozessor gehaltenen Daten den besonderen Typ der Prüfung anzeigt, die an den von der Platte getragenen Proben durchgeführt wird;

   wobei die Transportmittel Mittel zum Lesen der Etiketten enthalten, wodurch die Mikroprozessor-Steuermittel feststellen können, daß jeder aus dem Magazin genommene Träger geladen war und zutreffend ausgewählt wird, und die Gültigkeit anderer Bewegungen während des Prüfzyklus bestätigen können, und

   dadurch gekennzeichnet,

   daß die Transportmittel in der Lage sind, die Plattenträger in einer der Richtungen entlang jeder der x-, y- und z-Achse zwischen den

verschiedenen Arbeitsstationen zu bewegen, in einer Weise, die durch das Mikroprozessor-Steuergerät bestimmt wird, das zur Bestimmung der Reihenfolge, in der die verschiedenen Prüfungen durchgeführt werden, programmiert ist.

2. Gerät nach Anspruch 1, weiterhin enthaltend eine Übertragungsstation (10a), an der Platten gemessene Proben von biologischer Flüssigkeit empfangen, die durch eine automatische Pipettenanordnung (14) von einem Probenempfangsabschnitt (16) übertragen wurden.

3. Gerät nach Anspruch 2, worin der Probenempfangsabschnitt einen Leser (19) für maschinenlesbare Etiketten (18) auf Probenröhrchen (17) enthält, um zu bestätigen, daß diese korrekt im Probenempfangsabschnitt aufgenommen sind.

4. Gerät nach einem der vorhergehenden Ansprüche, weiterhin enthaltend eine Inkubatorstation (25).

Revendications

1. Appareil d'analyse de fluides biologiques dans lequel des échantillons mesurés de fluide biologique situés dans les puits d'une microplaque sont analysés, comprenant :

un dispositif de commande à microprocesseur (M) dans lequel peuvent être introduits des détails concernant les patients et différents tests requis,

une multiplicité de supports de plaques (11) discrets ;

un magasin (10) pour lesdits supports ;

une multiplicité de postes actifs comprenant :

un poste (23) dans lequel des réactifs chimiques sont ajoutés aux plaques par un dispositif de distribution de réactifs ;

un poste de lavage de plaques (26) ;

un poste de lecture de plaques (27) ;

un dispositif de transport de supports de plaques (20) qui est commandé par le microprocesseur pour prélever les supports de plaques dans ledit magasin et les faire progresser suivant les besoins parmi les postes actifs ;

chaque support de plaque comportant une marque d'identification unique (28) lisible à la machine qui, par référence aux données contenues dans le microprocesseur, indique le type particulier de l'analyse qui doit être réalisée sur les échantillons portés par la plaque ;

le dispositif de transport comprenant un dispositif pour lire lesdites marques de telle sorte que le dispositif de commande à microprocesseur peut vérifier que chaque support prélevé dans le magasin a été chargé et est choisi correctement et peut confirmer la validité des autres mouvements au cours du cycle d'analyse ; et

caractérisé en ce que le dispositif de transport est capable de déplacer les supports de plaques dans l'une ou l'autre direction suivant chacun des axes x, y et z entre les différents postes actifs d'une manière déterminée par le dispositif de commande à microprocesseur qui est programmé pour déterminer l'ordre dans lequel les différentes analyses sont accomplies.

2. Appareil selon la revendication 1, comprenant en outre un poste de transfert (10a) au niveau duquel les plaques reçoivent des échantillons mesurés de fluide biologique transférés depuis un poste de réception d'échantillons (16) par un dispositif à pipettes automatiques (14).

3. Appareil selon la revendication 2, dans lequel le poste de réception d'échantillons comprend un lecteur (19) pour des marques lisibles à la machine (18) de tubes d'échantillon (17) pour confirmer que ceux-ci sont chargés correctement dans le poste de réception d'échantillons.

4. Appareil selon l'une quelconque des revendications précédentes, comprenant en outre un poste d'incubation (25).

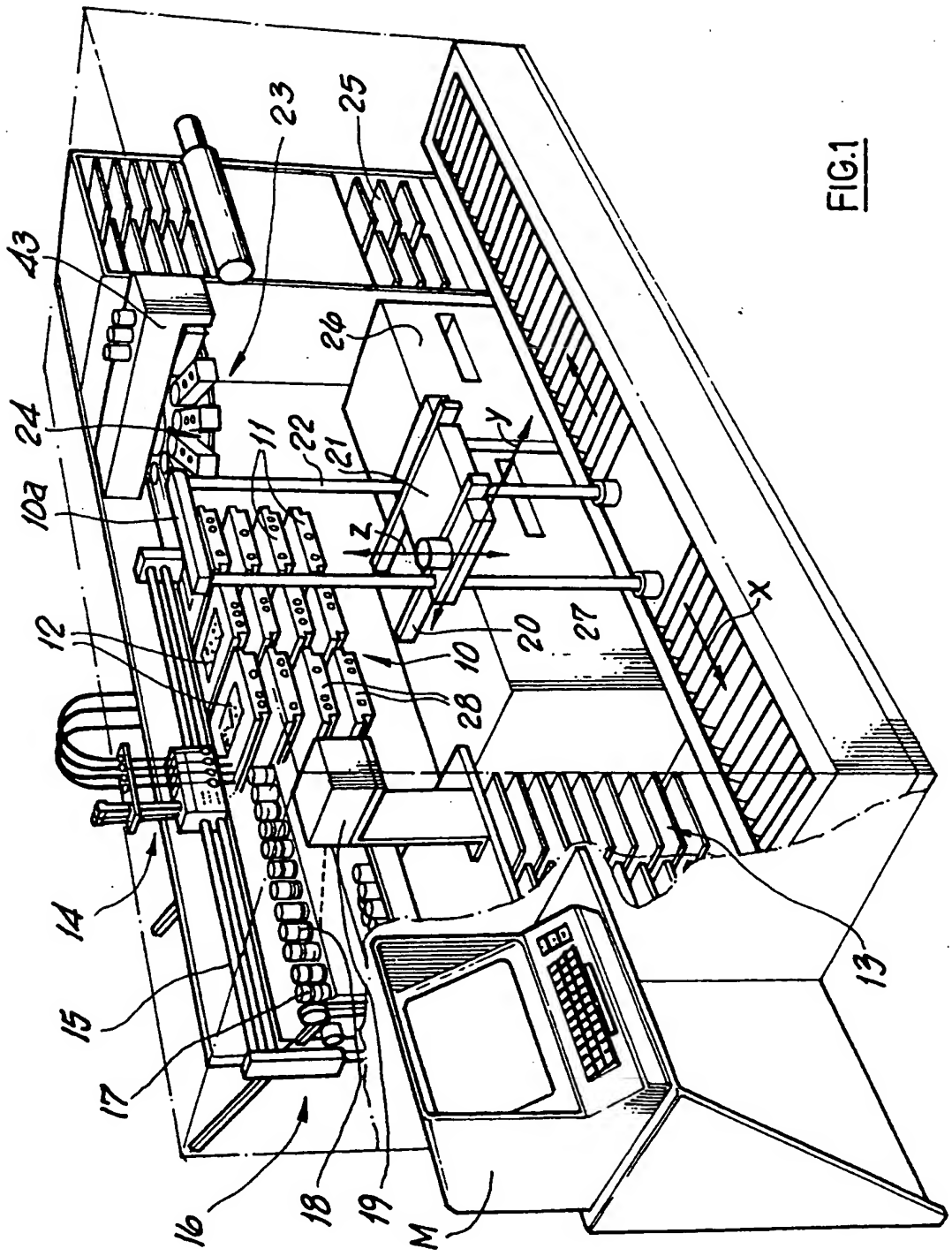

FIG.1

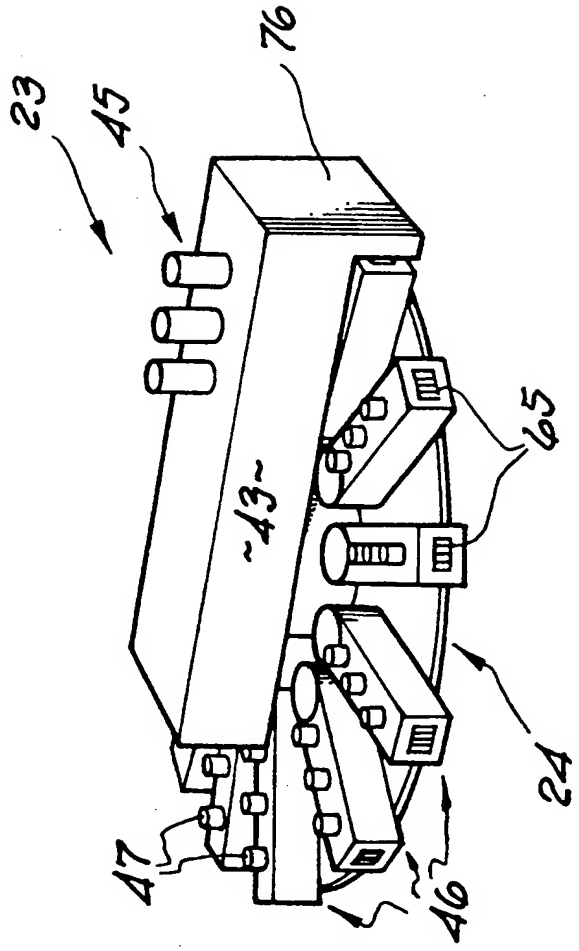

FIG. 2